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Reaction of the levoglucosenone Diels–Alder adducts with acetaldehyde under the McMurry conditions

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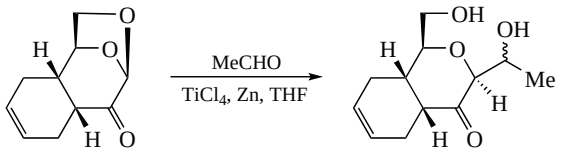
Reactions of acetaldehyde with Diels–Alder adducts of levoglucosenone with butadiene, isoprene, and cyclohexadiene assisted by low-valence titanium afford products of acetaldehyde addition to the acetal center with opening of the 1,6-anhydro bridge. In the case of the cyclopentadiene adduct, the reaction gives the product of addition of the ethyl substituent to the acetal center while the 1,6-anhydro bridge remains unchanged.

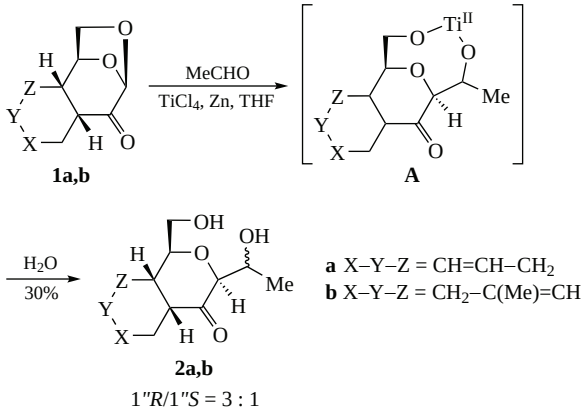


Keywords: levoglucosenone, Diels–Alder adducts, acetaldehyde, acetals, McMurry reaction, pinacol reaction.

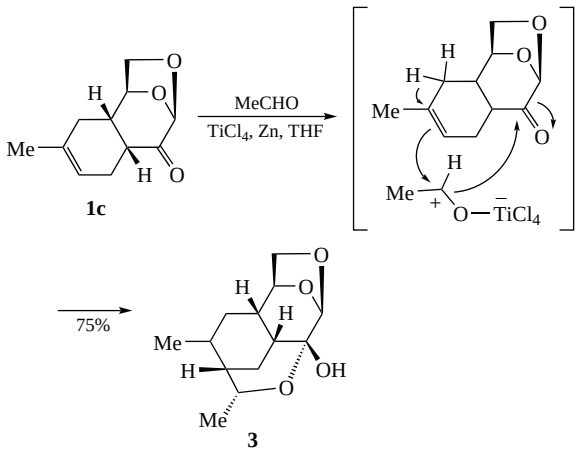
Diels–Alder adducts of levoglucosenone and 1,3-dienes contain two carbonyl centers, *i.e.* a keto group and a latent aldehyde group. Reactions with various nucleophiles mainly involve the free keto group.[1] Nevertheless, reactions that do not affect the keto group but involve the acetal center are known. Treatment of such adducts with NaI–Me_3SiCl system is accompanied by opening of the 1,6-anhydro bridge[2] and results in the selective reduction of the acetal center. Intramolecular cross-aldol reaction (after preliminary opening of the 1,6-anhydro bridge with Ac_2O–$ZnCl_2$) in the Michael adduct of levoglucosenone and cyclohexanone under the Mukayama reaction conditions involved the acetal center and gave a spiro compound.[3] Treatment of levoglucosenone–cyclopentadiene adduct with $SnCl_4$ caused intramolecular cationic cyclization at the acetal center accompanied by opening of the 1,6-anhydro bridge.[4] Based on these facts we assumed that it would be possible to perform the intermolecular pinacol synthesis under the McMurry reaction conditions in the presence of low-valence titanium.[5] Intramolecular reactions of this type are characteristic of dialdehydes, keto aldehydes and oxo esters.[5(*d*)] Less common intermolecular reactions are mainly used to obtain symmetric olefins from two molecules of aldehydes or ketones.[5(*d*),6] Reactions of this kind are unknown for derivatives of carbohydrates with an aldehyde group protected by a 1,6-anhydro bridge.

In this study, we anticipated of intermolecular coupling of acetaldehyde as the active substrate with the Diels–Alder adducts of levoglucosenone and 1,3-dienes when the $TiCl_4$–Zn system was employed to generate low-valence titanium.[7] However, the reaction outcome in general was found to be strongly substrate-dependent, namely, the structure of the preceding diene of the Diels–Alder adduct was crucial. In the common way the reactions of 'butadiene' **1a**[1(*a*)] or isomerized 'isoprene' **1b**[8] adducts proceeded to afford products of addition of acetaldehyde to the acetal center resulting in keto alcohols **2a**,**b** (Scheme 1). Apparently, the transformations occurred in agreement with the known mechanism[5(*d*),9] *via* intermediate **A**.

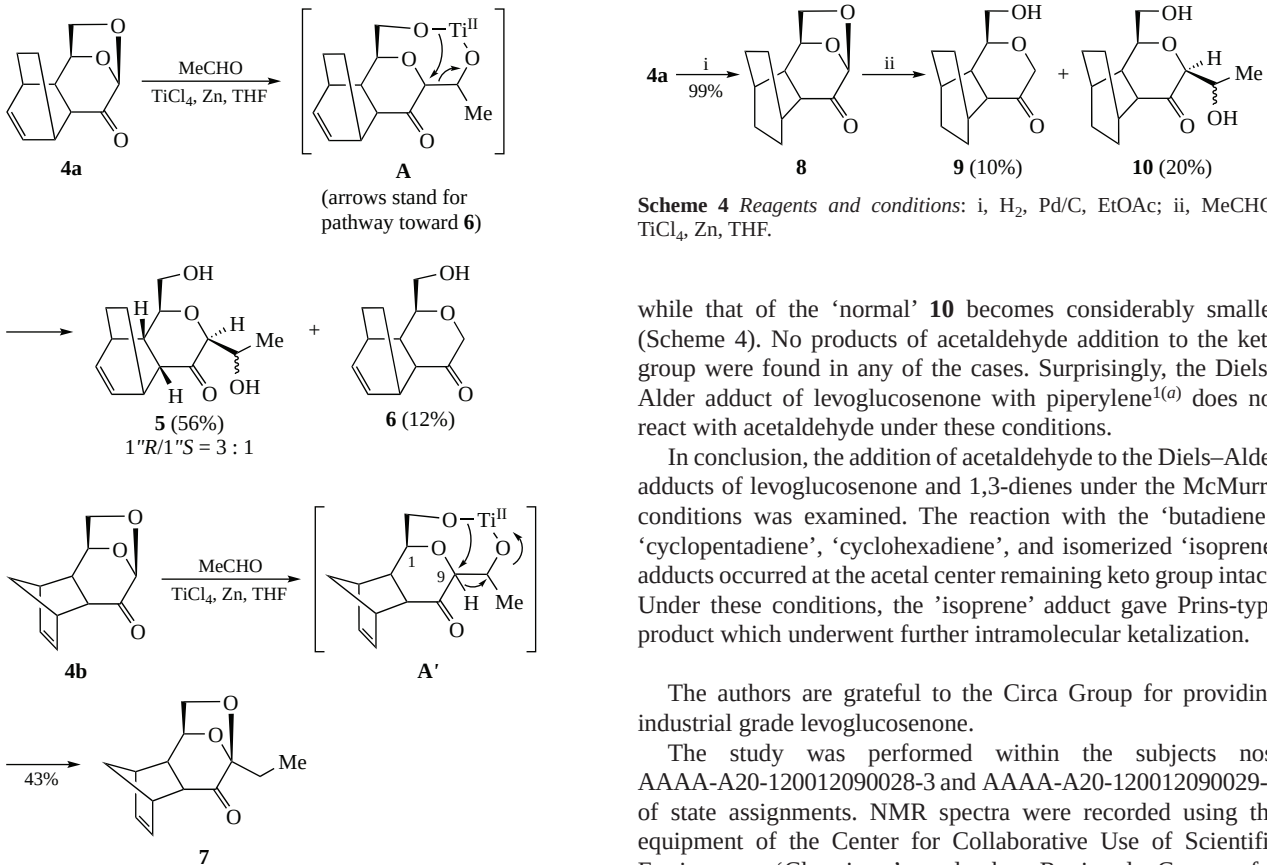
The reaction of the 'non-isomerized isoprene' adduct **1c**[1(*g*),(*h*)] with acetaldehyde resulted in semiketal **3** (Scheme 2). Most likely, at the first stage the Prins reaction between adduct **1c** and acetaldehyde occurs under the action of $TiCl_4$, accompanied by



Scheme 1 *Reagents and conditions*: **1a**,**b** (1.0 mmol), MeCHO (1.5 mmol), $TiCl_4$ (1.5 mmol), Zn (3.0 mmol), –10 °C, 12–72 h.



Scheme 2



Scheme 3

migration of the double bond. The transformation is finalized by the intramolecular addition of the latent hydroxy group at the keto function.

The reactions of 'cyclohexadiene' **4a** and 'cyclopentadiene' **4b** adducts[1(b),(c)] with acetaldehyde under similar conditions are shown in Scheme 3. Compound **4a** is transformed into product **5** structurally similar to **2a**,**b** (see Scheme 1) along with abnormal product **6**. Compound **6** most likely results from the reductive cleavage of the axial C–C bond in intermediate **A** accompanied by the opening of the 1,6-anhydro bridge. The formation of anomalous product **7** from substrate **4b** is most likely due to the proximity of the opposite sides of the molecule[1(b),(c)] and involves a 1,2-shift of H^9 in relative **A′** and recovering of the 1,6-anhydro bridge (see Scheme 3).

Most probably, the processes described above are also facilitated by the possible anchimeric assistance of the keto group through enolization of intermediate states. In the case of adduct **2a**, epimerization occurs at C^7 resulting in a mixture of four diastereomers. The formation of products **2a**,**b** and **5** can be alternatively explained by the aldol reaction that becomes possible after the 1,6-anhydro bridge is opened and, presumably, a enolate is generated in the presence of $TiCl_4$. An attempt to subject compound **4a** to any transformation under these conditions in the absence of acetaldehyde failed. The reaction of the dioxolane derivative of levoglucosenone[2] resulted only in its deprotection (see Online Supplementary Materials, Scheme S1), which is in agreement with published data,[10] while possible opening of the 1,6-anhydro bridge to give an intermediate semiketal did not occur. Hence, we cannot state that the reaction proceeds *via* the aldol condensation mechanism.

The presence of the remote double bond has a significant effect on the stabilization of the reaction intermediates. In fact, in the case of dihydro derivative **8** the product total yields decrease,

Scheme 4 *Reagents and conditions*: i, H_2, Pd/C, EtOAc; ii, MeCHO, $TiCl_4$, Zn, THF.

while that of the 'normal' **10** becomes considerably smaller (Scheme 4). No products of acetaldehyde addition to the keto group were found in any of the cases. Surprisingly, the Diels–Alder adduct of levoglucosenone with piperylene[1(a)] does not react with acetaldehyde under these conditions.

In conclusion, the addition of acetaldehyde to the Diels–Alder adducts of levoglucosenone and 1,3-dienes under the McMurry conditions was examined. The reaction with the 'butadiene', 'cyclopentadiene', 'cyclohexadiene', and isomerized 'isoprene' adducts occurred at the acetal center remaining keto group intact. Under these conditions, the 'isoprene' adduct gave Prins-type product which underwent further intramolecular ketalization.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2022.01.032.

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